Atty Dkt. No. 3831.08 Serial No.: 10/625,245

In the Claims

Claims 1-63 (canceled).

- 64. (Currently amended) The construct of claim 83 63 wherein said collagenous support matrix is prepared from a material selected from the group consisting of a Type I collagen; Type II collagen; and Type IV collagen; a collagen containing glycosaminoglycan, agarose or hyaluronin, a collagen containing proteoglycan, glycoprotein, gelatin, fibronectin, laminin, bioactive peptide, growth factor or cytokine, a collagen containing a synthetic polymeric fiber made of a polylactic acid, polyglycolic acid, polygmino acid or polycaprolactone, and a combination thereof.
- 65. (Previously presented) The construct of claim 64 wherein said support matrix is prepared from the Type I collagen.
- 66. (Currently amended) The construct of claim <u>83</u> 65 wherein said applied cyclic hydrostatic pressure is from about 0.5 MPa to about 5 MPa applied at a frequency of about 0.5 Hz for from about seven to about fourteen days followed by the resting period from about seven to about twenty-eight days.
- 67. (Currently amended) The construct of claim $\underline{83}$ 66 wherein said applied hydrostatic pressure is about 3 MPa applied at a frequency of about 0.5 Hz.

68. Canceled

Amendment e-filed: 3/6/08 3 of 24

- 69. (Currently amended) The construct of claim $\underline{83}$ 60 wherein said perfusion rate is about 5 μ 1/min.
- 70. (Currently amended) The construct of claim 83 63 wherein said activation of the chondrocytes of step e) is additionally performed under a reduced oxygen concentration is about 2% of less than 20%
- 71. (Currently amended) The construct of claim <u>83</u> 70 wherein additionally said activation of chondrocytes is performed at about 5% concentration of carbon dioxide.
 - 72. Canceled.
- 73. (Currently amended) The construct of claim $83\ 72$ wherein said support matrix has pores from of about 200 μm .
- 74. (Currently amended) The construct of claim 83 63 wherein said perfusion rate is from about 5 µl/min to about 50 µl/min.
- 75. (New) The construct of claim 83 wherein said inactive non-dividing chondrocytes are autologous.

Claims 76-82 Canceled.

83. (New) An implantable construct consisting essentially of a newly developed immature hyaline cartilage comprising a support matrix embedded with activated chondrocytes and an extracellular

matrix produced by said activated chondrocytes wherein a ratio of extracellular matrix to chondrocytes is lower than 95:5% and wherein said chondrocytes are rejuvenated chondrocytes activated from inactive non-dividing chondrocytes to activated chondrocytes by repeatedly applying to inactive non-dividing chondrocytes embedded in said matrix a cyclic hydrostatic pressure followed by a constant atmospheric pressure, wherein said activation results in cell proliferation, production of DNA and production of extracellular matrix macromolecules Type II collagen and S-GAG;

wherein said production of DNA is a result of genetic activation of said inactive non-dividing chondrocytes into active, dividing and multiplying chondrocytes able to propagate, proliferate and produce extracellular matrix thereby forming a newly developed hyaline cartilage within said support matrix,

wherein said Type II collagen and S-GAG are produced by the extracellular matrix synthesized by said activated chondrocytes,

wherein said inactive non-dividing chondrocytes are mature chondrocytes unable, without activation, to divide, multiply and synthesize the extracellular matrix macromolecules and wherein said chondrocytes are isolated from a human donor's joint cartilage by enzymatic digestion, expanded by culturing in a culture medium, suspended in a collagen containing solution, gel or thermoreversible hydrogel and seeded into the support matrix as a suspension of said inactive non-dividing chondrocytes.

wherein said support matrix is a sponge, scaffold, honeycomb or lattice, prepared from a material selected from the group consisting of a Type I collagen; Type II collagen; Type IV collagen; a collagen containing glycosaminoglycan, agarose or

Atty Dkt. No. 3831.08 Serial No.: 10/625,245

hyaluronin; a collagen containing proteoglycan, glycoprotein, gelatin, fibronectin, laminin, bioactive peptide, growth factor or cytokine; and a synthetic polymeric fiber made of a polylactic acid, polyglycolic acid, polyamino acid or polycaprolactone,

wherein said sponge, scaffold, honeycomb or lattice, each contains a plurality of pores having a size ranging from about 100 μm to about 300 μm ,

wherein said support matrix seeded with said inactive nondividing chondrocytes is subjected to the activation with a cyclic hydrostatic pressure from about 0.5 MPa to about 5 MPa above atmospheric pressure applied at a frequency of about 0.01 to about 2 Hz, for from about one hour to about 30 days, followed by a resting period at a constant atmospheric pressure for from about one day to about sixty days, such activation regimen repeated for from about one week to about three months,

wherein during said activation said support matrix seeded with said chondrocytes is further subjected to a perfusion with a perfusion medium at a flow rate from about 1 to about 50 μ L per minute,

wherein said activation of said chondrocytes is additionally performed under a reduced oxygen concentration of less than 20%,

wherein said activation results in converting said inactive non-dividing chondrocytes into activated chondrocytes that divide, multiply and synthesize said extracellular matrix macromolecules thereby forming said implantable construct, wherein said formed implantable construct comprises more than 5% of activated chondrocytes and a ratio of the newly synthesized extracellular matrix to activated chondrocytes is lower than 95:5,

Atty Dkt. No. 3831.08 Serial No.: 10/625,245

wherein said construct is implanted into a cartilage lesion and results in a full integration of said newly developed hyaline cartilage into a cartilage surrounding said lesion.

Amendment e-filed: 3/6/08 7 of 24